THE PUMP VS. THE “BUMP” — WHICH IS BETTER?

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INTRODUCTION

For nearly three-quarters of a century oral and maxillofacial surgeons have delivered intravenous anesthesia with an intermittent (incremental) bolus technique. The technique was popularized in the 1940s and 1950s by Dr. Adrian Hubbell and Harold Krough for the delivery of sodium pentothal anesthesia. Ultimately the agent utilized for intravenous anesthesia would change from sodium pentothal to methohexitol and finally from methohexitol to propofol. However, the method of delivery has varied little, with the possible exception of the use of somewhat smaller and more frequently administered increments of propofol as compared to methohexitol. During the same time frame, medical anesthesiologists found that a constant infusion with an infusion pump provided better working conditions, hemodynamic stability, and safety with the same level of patient satisfaction. However, as in their delay in adopting new anesthetic drugs, oral and maxillofacial surgeons have not been quick to adopt the newer method of anesthetic delivery used by their medical colleagues. In this review we will explore the pros and cons of the traditional intermittent bolus technique (Part I) versus constant infusions with an infusion pump (Part II) for office-based anesthesia in oral and maxillofacial surgery. The reader is encouraged to consult the original articles referenced to develop a more thorough understanding of the issues involved.

PART I: INTERMITTENT-BOLUS ANESTHESIA

by Mark F. Sosovicka, DMD

INTRODUCTION

Intermittent-bolus anesthesia for oral and maxillofacial surgery evolved in the 1930s and remains a simple, safe, and effective anesthesia technique. The overall anesthetic goals of patient safety, anxiolysis, hypnosis or sleep, amnesia and analgesia are fulfilled by the intermittent-bolus technique. Additional anesthetic goals, including immobility/muscle relaxation, inhibition of nociceptive and autonomic reflexes, antiemesis, a rapid return to physiologic and functional baseline, and acceptable costs are all attainable with the intermittent-bolus technique.

Any selected anesthetic technique should, first and foremost, be safe for the patient, of an appropriate duration to facilitate the surgical procedure, acceptable to the patient, and cost effective. For oral and maxillofacial surgeons intermittent-bolus anesthesia is effective for both the patient and surgeon for a number of reasons. Relevantly, the duration of the majority (93.3%) of oral and maxillofacial surgical procedures is under 60 minutes and most (63.8%) are completed in less than 30 minutes.1 The brief nature of most procedures affords the oral and maxillofacial surgeon the ability to provide a safe and effective anesthetic, most...
commonly utilizing an operator anesthetist model (90.9% of all OMFS providers), with a very low overall complication rate (0.7%).

We are fortunate as oral and maxillofacial surgeons to continue to provide safe and efficient anesthesia and surgical services to our patients, the result of our comprehensive training and our maintenance of high standards through continuing education and self-imposed peer review and inspection of our offices.

**HISTORY**

Lundy first utilized intermittent intravenous thiopental for general anesthesia at the Mayo Clinic in the early 1930s. Adrian Hubbell completed his oral surgical training at the Mayo Clinic and subsequently completed a 1-year anesthesia fellowship under Lundy before beginning to utilize IV thiopental for oral surgical procedures. The use of intermittent IV thiopental by Hubbell replaced the nitrous oxide hypoxic anesthetic technique that previously was a commonly utilized technique.

The use of intermittent IV anesthesia techniques by Hubbell and Krogh in the 1940s and 1950s began to develop. Jorgensen at Loma Linda introduced a multi-drug technique of pentobarbital, meperidine, and scopolamine for anxious dental patients in 1945 and became the “father of IV conscious sedation.” Hubbell and Krogh in the 1950s presented courses throughout the United States on the use of IV thiopental for dental patients. Hubble utilized a so-called intermittent pump technique. The “Hubbell Bubble” technique delivered a fixed dose of intermittent methohexital via a foot pump.

The mid-1950s saw a transition from conscious sedation to light general anesthetic techniques, and intermittent methohexital became the most commonly utilized IV anesthetic agent in the 1960s. In 1963, diazepam was introduced, and in 1970 fentanyl and ketamine were first used in an IV multi-drug regimen. The water soluble benzodiazepine, midazolam, was introduced in 1985, and propofol became available in 1989, ushering in the present day use of intermittent anesthetic agents for deep sedation/general anesthesia.

**Intermittent Bolus Goals**

The goals of intermittent anesthesia are to obtain a rapid induction of anesthesia and to maintain the anesthetic level with intermittent doses of anesthetic agent. Untoward side effects should be minimized, and the dosing is based on clinical parameters. The overall effects are dependent upon the patient’s age, sex, health status, and body composition. The effects are also altered by the baseline level of sedation set by the administration of narcotics, benzodiazepines, and possibly ketamine or other agents. Once a baseline level of sedation is established, sedative-hypnotic agents are utilized to maintain a state of deep sedation/general anesthesia.

The sedative hypnotic agents utilized to establish the deep sedation/general anesthesia generally have a rapid onset (20-60 secs.) and a similar metabolism (80-90% hepatic). The choice of agent is determined by a variety of factors, including drug effects (desired and adverse), patient profile, provider preference, cost and availability. Availability of drugs has
recently been a factor in anesthetic technique due to shortages of drug supplies. Drug shortages have been caused by manufacturing shortages, contamination with metal or glass particles, and drug companies’ discontinuing production due to medicolegal issues. Lawsuits have been brought against several drug manufacturers due to unsafe injection practices related to the use of multidose vials resulting in the spread of hepatitis and HIV.5

**Sedative Hypnotic Induction Agents**

The most often utilized sedative hypnotic induction agents include propofol, methohexital, ketamine, and dexmedetomidine. Thiopental was also previously used but is no longer available in the United States. This discussion will center on the induction agents propofol and methohexital. Ketamine can also be utilized as both an induction and maintenance agent, and dexmedetomidine, an alpha agonist with antihypertensive and sedative effects, has also been utilized as an induction agent.

Methohexital is an ultrashort barbiturate induction agent. Methohexital was first utilized in the 1960s with twice the potency and half the duration of thiopental. Methohexital is prepared as a 1% solution (10mg/ml) and has a rapid onset of 1 arm-brain circulation time of 40 seconds. This ultrashort duration is based on redistribution from the vessel-rich brain to muscle and fat, with little overall accumulation in fat tissue. Methohexital anesthesia lasts 5-7 minutes after injection and has a long elimination phase due to its slow metabolism in muscle and fat. Recently, there has been a resurgence in the use of methohexital due to intermittent propofol shortages.6

Untoward excitatory side effects of methohexital include hiccoughs, myoclonic movements, and possible seizure activity. Other untoward effects include tachycardia (usually 30% from baseline) due to baroreceptor-mediated sympathetic stimulation, dose-related hypotension, and overall cardiac depression. Arrhythmias may also arise in pediatric patients. Respiratory depression occurs and is dose-dependent; brief apnea following the induction dose is common. There is also a higher incidence of laryngospasm with the use of methohexital than with the use of propofol. Many of these side effects can be minimized by slow injection and an adequate baseline level of sedation with narcotics and benzodiazepines.6

Methohexital is epileptogenic and is utilized in the induction of psychiatric patients undergoing electroshock or electroconvulsive therapy.7 Barbiturates in general can have a “hangover” effect due to their slow metabolism with repeated doses and they will cause pain on injection. The use of a 1% solution limits the pain, but higher concentrations of methohexital result in more pain with vascular injection, a greater possibility of tissue necrosis with arterial injection, and increased undesirable muscle activity.6 Advantages of methohexital include its use for induction, maintenance of total intravenous anaesthesia (TIVA) for short diagnostic or surgical procedures, and the short duration of action that allows manipulation of anesthetic depth as dictated by the needs of the surgeon or patient.

Once reconstituted, methohexital is stable as a 1% solution and has a very basic pH of 10. Vials of methohexital are
commonly stored with refrigeration for up to 1 month with no bacterial growth. In contrast, propofol must be utilized within 6 hours once opened. However, the FDA does recommend that methohexital be utilized within 24 hours once reconstituted. Although the cost per mg of methohexital is greater than propofol, the common practice of storing methohexital for utilization for multiple anesthetic cases over an extended period of time can be a potential source of cost containment.6

Propofol is currently the most utilized sedative hypnotic induction agent due to rapid induction and recovery with minimal central nervous system effects. Di-isopropophenol (propofol) was introduced in 1985 and has become a standard induction agent both in the operating room and for ambulatory deep sedation/general anesthesia cases. Propofol can also be utilized as a maintenance agent for TIVA cases.

Propofol does have the drawback of having no analgesic properties. The drug has a rapid onset of 20-50 seconds and is short-acting with no clinical effects 30 minutes after discontinuing the drug due to its rapid redistribution, similar to what was described above for barbiturates.7 Propofol is highly lipophilic and has a large volume of distribution. Propofol has no active metabolites, has a rapid hepatic metabolism, and may also exhibit extrahepatic metabolism through the lung. Propofol does cause pain upon intravenous injection but this can be reduced by injection in a larger arm vein instead of a dorsal hand vein. The pain upon injection can also be reduced by administering lidocaine prior to the propofol or a fluid bolus following the propofol. Propofol has a pH of 7-8, undergoes oxidative degradation once a vial is opened, and does support bacterial growth due to its lipid emulsion of soya, glycerol, and egg lecithin. Therefore, it must be used within 6 hours of opening the vial.6

Propofol demonstrates first-order pharmacokinetics with a fast redistribution t1/2α of 2-4 minutes, a slow redistribution t1/2β of 30-60 minutes, and an elimination t1/2δ of 3-12 hours. Propofol’s pharmacokinetics are not affected by gender, hepatic cirrhosis, or renal failure.7 Propofol plasma level can be increased by the administration of other anesthetic agents. Propofol pharmacodynamically induces rapid sedation, hypnosis, and amnesia. Propofol induces the β subunit of the GABAA receptor, with possible inhibition of acetylcholine release in the hippocampus and pre-frontal cortex and possible inhibition of NMDA receptors.

Undesirable propofol effects include possible short-term hypotension, i.e., a 15% to 30% decrease in blood pressure. The degree of hypotension is related to the total dose and rate of propofol injection. Propofol-related hypotension is rarely a problem except in the elderly, hypovolemic patients, or patients with impaired left ventricular function. Propofol-related neurologic effects can result in excitatory phenomenon, such as muscle twitching or spontaneous movement in 14% of adults and 30% to 90% of pediatric patients. This increased muscle activity may resemble a seizure, including opisthotonus or back-arching rigidity, and has been termed propofol-related seizure-like phenomenon. Propofol-related infusion syndrome (PRIS) is rare and possibly fatal. It results in metabolic acidosis and rhabdomyolysis that is related
to long infusions, especially in pediatric patients.\textsuperscript{8} Propofol exhibits antiemetic properties and decreases the chance of post-operative nausea and vomiting with deep sedation/general anesthesia.\textsuperscript{7}

Propofol dosing is usually 1-3 mg/kg for induction and 20-100 ug/kg/min via infusion, and bolus dosing of 25-50 mg followed by additional 10-20 mg bolus doses as required by the patient’s vital signs or signs of light anesthesia.\textsuperscript{8,10} Propofol costs have increased over the last several years due to manufacturing and distribution shortages limiting availability of the drug.\textsuperscript{5} Some practitioners have recently utilized propofol-sparing techniques by administering other agents, such as greater doses of narcotics, benzodiazepines, and ketamine.

\textbf{Armamentarium and Setup}

The armamentarium and set-up for the intermittent-bolus technique are minimal. The set-up includes a basic IV administration set, 10-50cc syringes, and the desired drugs. The simple set-up usually requires no more than 1-2 minutes. In contrast, the set-up for a continuous infusion requires an infusion pump or pumps, an administration line in addition to the IV administration set, specific syringe brands and sizes in some cases based on the infusion pump utilized and a 3-way stopcock to refill the syringe in the infusion pump. The set-up time for the continuous infusion method is obviously greater because the syringes have to be loaded in the pump, the pump programmed and the administration line primed prior to use.

The costs of the intermittent-bolus technique are relatively minimal. The same supplies are utilized for each case, representing operating costs only with no initial capital costs. In contrast, the continuous-infusion technique requires initial purchase of the infusion pump, the cost for pump inspection and maintenance, and in some cases use of additional administration lines or syringes that may be specific to the pump utilized. Costs of infusion pumps generally range from $1,500 to $4,000, depending on the brand and features of the pump. Additionally, there is an increased cost-per-use associated with 1.7 ml to 7 ml of waste drug left in the tubing following the case. The lifespan of an infusion pump has been estimated to be 5-7 years, requiring replacement of the pumps following this time span adding to the capital costs.

The use of continuous-infusion pumps also has other drawbacks. Specific tubing and syringe brands may be necessary for the accurate use of specific infusion pumps. Different syringe manufacturers use different bore sizes for the same general size of syringe, and volumetric pump accuracy is sensitive to the internal diameter of syringe tubing. Neff, et al. have shown that small syringes, low flow rates, and compressibility of the syringe plunger affect the flow rate of infusion pumps.\textsuperscript{11}

Another factor is compliance, i.e., the change in volume with a change in applied pressure in the non-rigid components of the pump, such as the plunger or infusion line. Compliance has resulted in inadvertent overdoses when compression of the syringe plunger or infusion line blocked outflow, for example, someone standing on or compressing the infusion line attached to
the pump. When the occlusion is released the patient can receive an unintended bolus of drug, resulting in a change in depth of sedation or vital signs of the patient.8

Specific companies report approximately a 1% flow rate variation in the infusion pump and approximately a 3% variation when the infusion pump accuracy and the accuracy of the syringe attached to the pump are combined. These levels of variation are not generally a safety factor unless a pediatric or geriatric patient has increased sensitivity to medications that result in potential over-sedation or other untoward effects related to an overdose.9

Infusion pump maintenance and calibration is another cost factor with the use of infusion pumps that is not required with the intermittent-bolus technique. The Joint Commission on Hospital Accreditation and the FDA have specific written standards regarding the maintenance and calibration of automated equipment. Formal and documented maintenance and calibration programs must be implemented to ensure patient safety and should be performed every one to two years as a minimum.

In 2010, the FDA published a paper on errors or injuries during the use of automated devices, including infusion pumps. Most often, these were due to human error or from electronic or software malfunction. Obviously, the use of infusion pumps is not trouble-free or infallible, and their use has resulted in patient-related safety issues not encountered with the intermittent bolus technique.10

**INTERMITTENT-BOLUS TECHNIQUE**

The intermittent-bolus technique for propofol or methohexital relies upon a baseline anesthesia level which is established with opioids and benzodiazepines. Most commonly fentanyl is administered at 1µg/kg and midazolam is administered at 0.05 to 0.1 mg/kg for adult patients. These drugs are titrated by weight and clinical effect to provide anxiolysis and analgesia. Often ketamine is administered at 1-2 mg/kg as a neuroleptic agent to deepen the anesthetic level. Once the baseline level of anesthesia is established, the sedative-hypnotic agents (propofol or methohexital) are administered at 0.5-1 mg/kg by a bolus technique to induce general anesthesia; doses are based both on weight and on clinical effect. These agents place the patient in a state of deep sedation/general anesthesia requiring mandatory maintenance of the airway due to loss of protective reflexes.

Throughout the clinical procedure the desired level of anesthesia can be adjusted depending on the needs of the surgeon or the amount of clinical stimulation through the use of additional 10-30 mg boluses of propofol or methohexital. Dosage of all agents may have to be adjusted for age, sex, and body composition of the patient. Elderly patients generally are treated with a “low and slow” approach of drug administration due to their increased drug sensitivity and decreased drug clearance times whereas younger patients may require greater overall drug doses on a mg/kg basis.
The intermittent-bolus technique generally utilizes higher doses of the sedative-hypnotic agents during the initial administration of local anesthesia. Once adequate local anesthesia has been established, the intermittent doses of the sedative-hypnotic agent are decreased and are usually administered in response to changes in vital signs or other clinical signs (e.g., eye opening or vocalization) of an inadequate depth of anesthesia. Ultimately, the patient should experience intraoperative anxiolysis, amnesia, and analgesia while maintaining spontaneous ventilation.

Is the intermittent-bolus technique a safe and effective technique? Bennet and Shaffer, et al. compared the intermittent bolus versus continuous infusion propofol for dentoalveolar surgery. The hypothesis evaluated was that propofol by continuous infusion would result in lower propofol doses, a better surgical environment, and more rapid patient recovery than propofol by intermittent bolus. The study evaluated ASA I and II patients undergoing dentoalveolar procedures. All patients received baseline fentanyl and midazolam by weight and general anesthesia was induced by propofol administration of 1 mg/kg. Deep sedation/general anesthesia was maintained by either intermittent bolus or continuous infusion propofol. The intermittent-bolus group received additional propofol boluses of 10-30 mg. and the continuous-infusion group received a propofol infusion of 6 mg/kg/hr with additional boluses of propofol as needed based on the anesthetist’s observations of vital signs, movement, lacrimation, or vocalization.12

Recovery time was recorded and the surgeon and two observers rated the overall anesthetic by a visual analog scale. The surgeon and observers were not blinded to the anesthetic technique utilized. In the 16 cases evaluated the mean total dose of propofol by intermittent bolus was 6.03 mg/kg/hr and by continuous infusion was 7.93 mg/kg/hr. The number of boluses required were 3.6 per 10-minute interval by the intermittent-bolus technique and 1.1 per 10-minute interval with the continuous-infusion technique. Seventy-five percent of the continuous-infusion cases required bolus administration of propofol. Recovery time was slightly faster in the intermittent-bolus group than in the continuous-infusion group.

The surgeons and observers rated the continuous-infusion technique superior, although the technique used was not blinded. Both anesthetic procedures were rated satisfactory and all patients were amnestic to the surgery. The overall results did not support the initial hypothesis. The intermittent-bolus group used less propofol and had faster recovery times than the continuous-infusion group. More importantly, the continuous-infusion group required additional boluses of propofol, showing the technique is not “a hands-free technique” once the continuous infusion has been started.12

Other studies had similar results. As recently as 2012 a Cochrane collaboration study evaluated target-controlled infusion versus manually-controlled infusion of propofol for general anesthesia or sedation in adults. The study reviewed 20 trials involving 1,759 patients to evaluate whether a target-controlled infusion is as effective as a manually-controlled infusion of propofol
The Pump vs. the “Bump”

Richard C. Robert, DDS, MS & Mark F. Sosovicka, DMD

for general anesthesia and sedation with respect to anesthesia quality, adverse events, and overall propofol drug costs. The target-controlled infusion was associated with greater overall propofol doses and costs than manual infusion and there were no clinically significant differences in the number of adverse events between techniques. Clinical anesthetic quality did not differ significantly in terms of bispectral index values, recovery time, and patient, surgeon, and anesthetist satisfaction. The authors concluded that overall results of the systematic review did not provide significant evidence to recommend target-controlled infusion versus manual-controlled infusion of propofol for clinical anesthesia.

Klein, et al. compared propofol administered by continuous infusion versus bolus in pediatric patients undergoing ambulatory oncologic procedures such as bone marrow biopsy or line insertion. All patients received an induction bolus of propofol at a dose of 0.5 mg/kg; this was followed either by a continuous infusion of 0.1 mg/kg/min. (increased by 20% until induction) or additional intermittent boluses of 0.5mg/kg until achievement of deep sedation/GA. There were no differences in induction doses or induction time, recovery time, or adverse events. As expected, more boluses were delivered in the bolus group (8.5) than in the continuous-infusion group (5.4). However, the total propofol dose was higher in the continuous-infusion group than the bolus group (8 mg/kg versus 5.8 mg/kg). Both the continuous infusion and bolus techniques were satisfactory to the patient and surgeons. Ultimately physician preference will dictate which method will be used in the future.

Candelaria and Smith also evaluated the use of a propofol infusion technique for out-patient general anesthesia during dentoalveolar surgery. Their study evaluated the use of alfentanil 10µg/kg, nitrous oxide, and propofol at 1 mg/kg for induction followed by continuous infusion of propofol at 150 µg/kg/min. No midazolam was used. Any movement to surgical stimulus was treated with a propofol bolus of 10 mg. All patients were induced under general anesthesia in less than 1 minute and all patients had anterograde amnesia. No excitation, tremors, or hypotonus were noted and the vital signs were stable. The average case was 22 minutes in length for induction and completion of the surgical procedure. The optimal infusion rate was 150 µg/kg/min and the average total propofol dose was 350 mg. Patients received an average of 2 propofol bolus doses, with a range of 0 to 5.

The overall assumptions that continuous variable-rate infusions decreased the amount of propofol administered and that using a pump for continuous infusion allows the surgeon to direct attention to the surgical field without repeat interruptions to provide additional boluses with the bump technique were not supported. Obviously the total overall propofol dose was rather high and the procedure was not completely hands-free once the infusion was started; an average of two additional propofol doses were administered to the patients in this study.

HOW DEEP IS DEEP ENOUGH?
Questions often arise concerning the overall depth of anesthesia and whether all patients require a continuous infusion to maintain a deep anesthetic state. The depth of anesthesia is determined by the needs of the patient and the surgeon. Most surgical procedures can be performed in a safe and efficient manner under deep sedation, and some movement is generally tolerable with most dentoalveolar procedures based on the surgeon’s overall skills and experience. An excellent study of factors that influence patient satisfaction or dissatisfaction with office-based deep sedation/general anesthesia were evaluated by Coyle, et al.16 The study evaluated over 14,000 patients who had deep sedation/general anesthesia for dentoalveolar surgery.

The overall satisfaction rate was 95.8%, leaving little room for improvement. Interestingly, when patients received deep sedation/general anesthesia with local anesthesia, a narcotic, and a benzodiazepine but no propofol, methohexitol, or ketamine they had greater overall satisfaction than when propofol, methohexitol, and ketamine were utilized (96.4% versus 95.6% satisfaction). Unexpectedly, providing a deeper anesthetic level did not improve the overall patient satisfaction with the anesthetic procedure. The addition of nitrous oxide to the deep sedation/general anesthesia with local anesthetic, a narcotic, and a benzodiazepine

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<thead>
<tr>
<th>TABLE 1: COMPARISON OF ANESTHETIC TECHNIQUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMITTENT BOLUS TECHNIQUE</td>
</tr>
<tr>
<td>Set up time:</td>
</tr>
<tr>
<td>Overall armamentarium:</td>
</tr>
<tr>
<td>Initial equipment start-up costs:</td>
</tr>
<tr>
<td>Specific syringes or IV tubing needed:</td>
</tr>
<tr>
<td>Periodic equipment calibration or maintenance</td>
</tr>
<tr>
<td>Need for periodic equipment replacement:</td>
</tr>
<tr>
<td>Opportunity for human error:</td>
</tr>
<tr>
<td>Opportunity for equipment malfunction:</td>
</tr>
<tr>
<td>Totally hands-free anesthesia technique:</td>
</tr>
<tr>
<td>Lower overall drug use:</td>
</tr>
<tr>
<td>Overall anesthetic costs:</td>
</tr>
<tr>
<td>Acceptable overall anesthetic quality:</td>
</tr>
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did improve overall patient satisfaction (96.3% versus 95.8%). Additionally, the use of steroids with the sedation had no effect on overall patient satisfaction.16

Placing the patient in a deeper anesthetic state did not improve overall patient satisfaction and was possibly performed to comply with the desires or expectations of the operating surgeon rather than the desires or expectations of the patient because most patients had no recall of the procedure. Certain factors were predictors of dissatisfaction, including patient age less than 10 years, vomiting during recovery, remembering pain during the procedure, and a memory of being awake with inability to communicate. The result that the use of propofol, methohexital, or ketamine did not improve overall patient satisfaction reinforces the belief that anesthetic depth is not a predictor of patient satisfaction.16

CONCLUSIONS

The intermittent-bolus anesthesia technique is simple, with minimal equipment, no equipment maintenance, low overall costs, quick set-up, and low potential for mistakes due to dosing or set-up errors. The intermittent-bolus technique has been and remains an effective anesthetic technique for out-patient oral and maxillofacial surgical procedures.

PART II: CONTINUOUS INFUSION WITH AN INFUSION PUMP FOR OFFICE-BASED SURGERY IN OMS

by Richard C. Robert, DDS MS

INTRODUCTION

The Early Years

The inestimable contributions of dentists to the history of anesthesia are undeniable. The very foundation of surgical anesthesia can be traced to dentists Horace Wells and William T.G. Morton, who in the 1840s discovered the anesthetic properties of nitrous oxide and ether respectively. These inhaled gases were to remain the principal agents in anesthesia for the next century.17 However, “anesthesia” based on anoxic levels of nitrous oxide anesthesia would ultimately be toppled by two other dental anesthesia pioneers: Californian Adrian Hubbell and his East Coast colleague, Harold Krough, promoted sodium pentothal-based intravenous anesthesia in the mid-twentieth century.3 Sodium pentothal also began to gain considerable attention in medical anesthesia during and after the Second World War.

Interestingly these early pioneers realized that the intermittent-bolus technique prevented the maintenance of a constant plasma level of anesthetic and hence a smoother anesthetic course. Indeed, in an attempt to circumvent loading and delivering drugs with syringes, Hubbell invented the “Hubbell Bubble”, a rubber bulb that could be frequently activated by a “human pump” (the operator’s foot) in order to achieve as
constant a plasma concentration as possible.18 Similarly, medical anesthesiologists utilized “piggy-back” micro-drips of anesthetic agents in an attempt to maintain a constant infusion.19

Although oral and maxillofacial surgery offices were the predominant venue for office-based anesthesia at mid-century, our medical colleagues were ultimately to appreciate the advantages of providing anesthesia on an outpatient basis without the need for lengthy, expensive hospital stays. By the latter decades of the century, 75% of what had been formerly predominantly hospital inpatient surgery found a home in a variety of ambulatory venues, including outpatient surgery centers and surgeons’ offices.20

As medical anesthesiologists developed their appreciation for the outpatient setting, they realized that the intravenous and inhalation agents at their disposal would be a primary limiting factor. Pharmaceutical companies, sensing new and profitable markets, poured R&D funds into the development of new agents that would allow the patient to become “street-ready” as rapidly as possible. The longer-acting benzodiazepine diazepam would soon be replaced by a shorter-acting water-soluble benzodiazepine, midazolam.21 Similarly, the longer-acting but well established synthetic phenylpiperidine opioid meperidine was soon replaced by the shorter-acting anilidopiperidine fentanyl.22 Then in the final decade of the century, the ultra-short-acting barbiturates thiopental and methohexital were eclipsed by an even shorter-acting major hypnotic agent, propofol.23

Although each of the advances of the latter decades of the last century were warmly embraced by medical anesthesiologists, for inexplicable reasons the pioneering spirit of oral and maxillofacial surgeons (and dentists in general) appeared to wane. They clung to meperidine, diazepam and methohexital even as newer shorter-acting agents became well entrenched in the armamentarium of anesthesiologists in outpatient surgery centers and office-based anesthesia.

It was not until the first decade of the present century that the shorter-acting agents began to make definitive inroads into oral and maxillofacial surgery offices. Perhaps the most dramatic change was prompted by the so-called “Brevital Crisis” when methohexital production came to a halt because of contamination at its major production facility.24 With methohexital no longer available oral and maxillofacial surgeons were forced to turn to propofol. This lead to a “Eureka experience”, which prompted most surgeons to continue to use their new found anesthetic ally even when methohexital came back on the market.

A similar reluctance to embrace newer shorter-acting agents is seen when one looks at the method of delivery most commonly used by oral and maxillofacial surgeons versus their medical colleagues. The same scientific approach that enabled medicinal chemists to develop new short-acting agents laid the foundation for use of constant-infusion technology for anesthetic delivery. Yet oral and maxillofacial surgeons continue to hold tightly to the intermittent-bolus technique, which was developed three-quarters of a century ago, long after scientific discoveries
prompted medical anesthesiologists to largely abandon the bolus technique in favor of constant-infusion technology that could capitalize on the most desirable attributes of the newer drugs. In this section I will explore their reasons for their making the change and examine a number of the factors that prompted their decision, including:

1. The foundation in scientific research that supports one vs. the other.
2. The quality of operating conditions afforded by using the different techniques.
3. Patient satisfaction with the technique utilized.
4. The hemodynamic stability provided by the technique.
5. The safety afforded the patient by use of the technique.
6. The convenience and expense associated with the technique.

**SCIENCE LEADS THE WAY**

In the latter part of the twentieth century, while oral and maxillofacial surgeons became complacent with their methohexital-based intermittent bolus technique, considerable scientific investigation prompted anesthesiologists to begin using constant infusions with infusion pumps for their ambulatory surgery procedures.

**The Receptor Concept**

At the beginning of the twentieth century events took place that would ultimately change the entire foundation of the field of pharmacology. Langley and Elliot’s laboratories at Cambridge University in the United Kingdom, as well as Ehrlich’s laboratory in Frankfurt, Germany, established that the action of most drugs is due to the binding of the drug molecules to protein molecules within the host (“receptors”). Although this concept formed the basis for countless pharmacologic investigations during the next three-quarters of a century, the receptor concept did not become commonly accepted in anesthesia circles until the 1980s. Up until that time the theory of “lipoid solubility”, propounded by Myer and Overton was regarded as the overriding mechanism of anesthetic agents. This theory was based on the concept that the action of anesthetic agents was due to their dissolution in the membrane of neurons that prompted a physical change such as thickening of the membrane, which in turn altered the permeability of the membrane to ions. It was postulated that this permeability change produced the anesthetic effect.

Ultimately, in the 1990s, this theory was overturned by the work of Franks and Lieb showing that the action of anesthetic agents is based upon the binding of anesthetic molecules to host receptors. This revelation facilitated investigation of rapidly-acting agents with short duration such as propofol. It was demonstrated that propofol had an affinity for a site on a chloride ion channel, i.e., the same gamma-aminobutyric acid (GABA<sub>A</sub>) receptor ion channel targeted by benzodiazepines. (Fig. 1, P. 14) In turn, the short duration of the bond with
rapid redistribution of the agent meant that sustaining the effect would be most effectively achieved by constant "bathing" of the receptor with the agent, something only accomplished with a constant infusion. Frequent intermittent boluses could approach but never duplicate this effect.

A particularly fascinating characteristic of propofol is the unusual manner in which it reacts with the different GABA<sub>A</sub> receptor subtypes. Classic GABA<sub>A</sub> receptors contain five subunits: two α-subunits, two β-subunits, and one γ-subunit. (Fig. 2) At least three subtypes of the β-subunit have been identified and they are designated as β<sub>1</sub>, β<sub>2</sub>, and β<sub>3</sub>. When propofol is given at higher doses, it induces a level of deep hypnosis and immobilization through its binding to receptor sites on those GABA<sub>A</sub> receptors that contain the β<sub>3</sub>-subtype.29 However, at lower doses propofol targets receptors containing β<sub>1</sub> and β<sub>2</sub> subtypes, facilitating the action of GABA in a manner somewhat similar to that seen with benzodiazepines. Thus, propofol can be used for both the induction and maintenance of anesthesia, as well as sedation.30

In the latter setting it has found application for management of the elderly, the medically compromised, patients with obesity and obstructive sleep apnea and patients who undergo longer procedures for which a lighter level of sedation is required, such as complex implant cases. This lighter level of sedation is much more practically achieved with a low-level, continuous infusion than with very small intermittent boluses timed appropriately to maintain the level of minimal to moderate sedation.

**The Blood-brain Barrier**

Investigations into the nature of the blood-brain barrier during the latter decades of the twentieth century pointed to two primary factors determining passage of drugs through the barrier to exert anesthetic effects on the
The Pump vs. the “Bump

Richard C. Robert, DDS, MS & Mark F. Sosovicka, DMD

Figure 3: The endothelium of the blood brain barrier has tight junctions which allow paracellular passage of only small molecules such as those of propofol and methohexital. In addition, the end feet of the astrocytes cover much of the circumference of the capillary.

Figure 4: Conceptualization of a three compartment model which takes into account the complex pharmacokinetics of highly lipid soluble drugs such as propofol ketamine and remifentanil. Source: 33, Page 26 Fig.3

As more highly lipophilic, rapidly-redistributing drugs became available, it was realized that some of the parameters previously utilized in pharmacokinetics were inadequate to describe the complexities of the fate of anesthetic agents in the body. In particular, the concept of elimination half-life did not take into account the dynamic relationship between redistribution and drug clearance. It became apparent that redistribution was largely dependent upon circulation differences in various types of the body’s tissue. Investigators divided the various tissues into artificially designated “compartments” based on vascularity. A model for drug distribution was developed based on a vascular-rich group, a vascular-poor group and an intermediate group. As drug molecules were differentially distributed through the various groups, they would ultimately return to the central compartment at different times and then be subject to biotransformation and elimination. (Fig. 4)

To adequately describe this dynamic interplay between the agents and the body’s
tissues a new parameter, the “context-sensitive half-time”, was introduced. Calculated with mathematic models based on pharmacokinetic studies, it represents the time required for the plasma concentration of the drug in question to decline by 50% once the infusion has been terminated.34 This is an important parameter because it provides uniform comparison of the behavior of different drugs that affect their clinical attributes (Fig. 5). For example, it explains why recovery from a propofol-based anesthetic is more rapid than that from methohexital and dramatically more rapid than that from thiopental.

However, capitalizing on this parameter is more likely if a constant level of agent is being introduced into the system by a constant infusion, clinically manifested by a “smooth” anesthetic course with minimal tendency toward patient movement and response to surgical stimulation. With intermittent delivery the dynamic interplay discussed above would tend to accentuate peaks and troughs of agent concentration in the serum.

**Biotransformation and Elimination**


The newer lipophilic and rapidly-redistributing drugs developed in the latter decades of the 20th century also tended to undergo rapid biotransformation and elimination. Hepatic biotransformation of propofol is rapid but it is also accompanied by biotransformation in other body tissues, especially the lungs.35

In addition, medicinal chemists developed a new approach to drug biotransformation. It was found that incorporation of certain forms of chemical linkage could enable drug biotransformation in tissues other than the liver. For example, in the case of remifentanil the anilidopiperidine base is linked to a side chain with an ester linkage, and biotransformation takes place through enzymatic cleavage of the ester link. (Fig. 6, P. 17) Because esterases are present in virtually all body tissues, biotransformation takes place much more rapidly than that of other opioids, for which the biotransformation takes place only in the liver.36

The rapid metabolic pathways of drugs
The Pump vs. the “Bump”

Richard C. Robert, DDS, MS & Mark F. Sosovicka, DMD

Figure 6: Comparison of the chemical structures of fentanyl and remifentanil. The ester linkage illustrated enables biotransformation by esterases found throughout the body.

such as propofol and remifentanil worked hand-in-hand with rapid redistribution to create very low, flat plots of context-sensitive half-time (Fig. 5). This, in turn, is reflected in the rapidity and completeness of recovery with these agents.

The Agents

Obviously a primary requisite of office-based or ambulatory anesthesia is the ability to render the patient street-ready as rapidly as possible so that recovery at home can continue both comfortably and safely. The quantitative parameter that comes closest to equating with rapid, yet safe, patient discharge is the context-sensitive half-time discussed above. A low, flat plot suggests that the drug’s effects (especially untoward ones such as respiratory depression) dissipate rapidly and do not return, even after protracted infusion.37

When one views the plots of the various agents that have been used for ambulatory and office based anesthesia, three stand out: propofol, remifentanil and ketamine. (Fig. 5, P. 16) In medical anesthesia, all three of these agents have been successfully used and enjoy wide popularity. In oral and maxillofacial surgery, propofol is the primary agent used in the vast majority of offices, with ketamine finding an ever-increasing role. Remifentanil has piqued interest in some practitioners but is still infrequently utilized.38

As pointed out above, propofol interacts with the GABA<sub>A</sub> receptor in two different ways such that it can be utilized for both sedation as well as induction and general anesthesia. Soon after its introduction in the United Kingdom, studies began to emerge about the successful use of propofol for sedation. In 1987, Mackenzie and Grant reported that “recovery is impressively rapid, even in elderly patients, and devoid of side effects.”39

Although the “gold standard” for amnesia associated with anesthetic agents is the benzodiazepines, it appears that propofol may have some amnestic properties as well. In 1997, Veselis concluded that when the agents are used for sedation, propofol produces the same degree of amnesia as midazolam while thiopental provides very little and fentanyl no amnesia at all.40 Furthermore, Tesniere found that when propofol was used in low concentrations, its respiratory effects were moderate, and it allowed spontaneous ventilation throughout maintenance of sedation.41 Thus, there is good support for use of propofol for sedation in the elderly, the medically compromised and for patients undergoing longer procedures. Administering it in low concentrations is challenging without
the use of an infusion pump to provide a consistently low serum level of the agent.

Because each of the agents propofol, ketamine and remifentanil produce a desirable low, flat context-sensitive half-time plot, the possibility of using them in combination was too great for investigators to resist. Rama-Maceiras, et al. found that using remifentanil with propofol significantly decreased the incidence of post-operative nausea and vomiting compared to fentanyl. Numerous studies have reported good results with the propofol-remifentanil combination, and in 2009, Eikaas and Raeder concluded that propofol with remifentanil was emerging as the most popular technique for total intravenous anesthesia. The caveat was that each of the drugs must be administered by continuous infusion.

Another intriguing combination of the new agents has been the simultaneous administration of propofol and ketamine, capitalizing on the complementary effects of the two drugs. For instance, the hypotension that accompanies administration of propofol is counter-balanced by the increase in blood pressure and pulse from the admixed ketamine. Similarly the tendency for dysphoria, often associated with ketamine administration when it is given alone, is largely overcome by the euphoria imparted to the mixture by propofol. The admixture is most commonly administered by infusion pumps in medical anesthesia and in some studies in the oral and maxillofacial surgery literature as well.

Providing Ease of Administration - Technology

Over the last several decades, as advancements in medicinal chemistry brought newer, more desirable drugs to the marketplace, technology based on microchips advanced even more rapidly. This explosion of technologic advancement made possible computer-driven server mechanisms that allow various pieces of apparatus to be controlled by computers. This technologic advancement soon found its way into the field of anesthesia with the introduction of much improved infusion pumps. Although large cumbersome infusions pumps had been available during previous decades, the new devices incorporating microchip technology supplanted their predecessors rapidly.

One of the first of these devices, originally developed by Bard (C.R. Bard, Inc., Murray Hill, New Jersey) in the late 1980s, was sold to Baxter (Baxter International Deerfield, Illinois) in the early 1990s and became the Baxter Infuse O.R. pump that was to dominate infusion pump technology over the next couple of decades. It was a hybrid analog-digital device with an internal drive mechanism that relied on separate electromagnet templates to control the individual drugs. Setting the parameters for medication delivery was accomplished with a simple and exceedingly intuitive programming panel containing four dials. (Fig. 7 on P. 19)

Although Baxter ultimately discontinued manufacture of the Infuse O.R. pump, its popularity has remained unabated. The unit continues to be in high demand in hospitals, outpatient surgery centers and in oral and maxillofacial surgery offices as well. As the demand persisted, refurbished units returned
The Pump vs. the “Bump

Richard C. Robert, DDS, MS & Mark F. Sosovicka, DMD

Figure 7: The Baxter Infuse O.R. infusion pump, a hybrid analog-digital device popular for many years but no longer in production. Refurbished units continue to be used widely in ambulatory surgery and office-based anesthesia.
Source: Courtesy of Richard C. Robert, DDS, MS, South San Francisco, CA.

Newer-design pumps incorporate extensive “smart technology” based on microprocessor technology. The syringes continue to be driven by a screw mechanism, with the control of the servo-motor directed by extensive drug libraries containing settings for large numbers of agents and administration parameters. (Fig. 8) The pumps can even “sense” the type of syringe in the pump cradle to assure that the drug-administration settings match those of the syringe through which the drug will be administered. Newer pumps also have a confirmation mode such that the settings for each patient must be confirmed, assuring that settings used for a previous patient are not inadvertently used for the current one.38

Because computer modeling can be successfully utilized in assessing the pharmacokinetic properties of various agents with the context-sensitive half-time, investigators attempted to take the process one step further. Computer models were developed for the maintenance of a continuous serum concentration of drug, a so-called “target-controlled infusion” system. The TCI concept took hold in countries throughout Europe.13,46-53 However, both the FDA in the United States and the Canadian authorities found that TCI devices were not sufficiently advantageous to approve their commercial
The Bottom Line

By the middle of 1990s, with excellent short-acting drugs available, a better understanding of how the drugs worked, and compact “user-friendly” infusion pumps, medical anesthesiologists set out to document the superiority of operating conditions, street readiness of their patients and satisfaction of the patients with their anesthetic experience. Miller summarized the rationale for use of a continuous infusion:

“Administration of IV anesthetic drugs by infusion provides for greater stability of drug concentration within the plasma and hence at effector sites, than can be achieved with an incremental bolus technique... Infusion techniques thus tend to provide a smooth intra-operative course characterized by enhanced cardiovascular stability, and with appropriate titration, facilitate rapid and uneventful emergence from general anesthesia...Other potential advantages include a lower incidence of side effects, shorter recovery times, and decreased drugs costs.”

MAXIMIZING OPERATING CONDITIONS

For an anesthetic experience to be successful, the surgeon must be satisfied with the operating conditions and the patient satisfied that he was as comfortable as possible under the circumstances. In this section we will address the former and in the next section the latter.

Providing Surgeon Satisfaction

Even before propofol became available in the US, investigators were exploring the differences between incremental bolus and continuous infusion techniques. In 1983, in a cohort of 100 patients, White compared intermittent bolus administration to a continuous infusion utilizing ketamine-based and fentanyl-based intravenous anesthetics. He concluded that “continuous infusion... improves intra-operative conditions, and decreases recovery time compared with a traditional intermittent bolus technique.” In a study comparing the two approaches for opioid-based anesthetics utilizing fentanyl and alfentanil, White, et al. concluded “the use of a continuous infusion (vs. intermittent injection) of alfentanil allows the anesthetist to titrate the dose of drug with greater precision.”

From studies conducted in Europe in the mid 1980s, it became apparent that a total intravenous anesthetic based on propofol could be used for ambulatory anesthesia. In 1988, Price, et al. compared a total intravenous anesthetic utilizing fentanyl and alfentanil, White, et al. concluded “the use of a continuous infusion (vs. intermittent injection) of alfentanil allows the anesthetist to titrate the dose of drug with greater precision.”

By the mid 1990s, propofol had become the preferred agent for ambulatory anesthesia in medicine. Studies continued to assess differences between anesthetics delivered
by intermittent bolus techniques versus a constant infusion. In 1995, Newson, et al. summarized their conclusions in comparing the two techniques indicating that the “The anesthesiologist had to intervene more frequently in the intermittent bolus injection group rather than in the two infusion groups. We conclude the use of the infusion technique may allow the anesthesiologist more time for monitoring the patient by decreasing the number of interventions necessary to administer supplemental doses of sedative medication during the operation.”

During the 1990s, oral and maxillofacial surgeons also began to explore the possibility of using propofol for office-based anesthesia. Candeleria and Smith noted wide fluctuations in cardiorespiratory and psychomotor activity in intravenous techniques utilizing the incremental bolus technique. In a study of 21 ASA I patients undergoing short-duration OMS procedures in an office setting they concluded that “using a pump for continuous infusion allows the surgeon to direct attention to the surgical field without repeated interruptions to administer the drug bolus required with the bump technique” and “... an infusion pump enables achievement of a sustained sedative-hypnotic effect without oscillations between peak and trough levels in the blood and brain, producing varying levels of anesthetic depths.”

In 1998, Bennett, et al. compared an incremental bolus technique to a continuous infusion technique of propofol in a cohort of 39 ASA I and II patients. Although both techniques were found to provide “satisfactory conditions,” they concluded that “The continuous infusion of propofol was associated with an anesthesia level that was statistically superior in both minimizing patient movement and providing a more optimal overall quality of anesthesia.”

By the end of the 1990s and the beginning of the first decade of the 21st century, the evidence was mounting that the incremental bolus technique could not provide the same optimal surgical conditions that could be achieved with a pump-administered continuous infusion. In fact, it even appeared that a continuous infusion of a propofol-based anesthetic could provide surgical conditions equal to or superior to those provided by a traditional balanced anesthetic with isoflurane and alfentanil. In 2003, Everhart, et al. reported on such a comparison in a cohort of 90 consecutive patients undergoing microscopic and endoscopic sinus surgery. They concluded: “Intravenous anesthesia using propofol-remifentanil provides better surgical conditions compared with a traditional balanced anesthetic technique utilizing isoflurane-alfentanil.”

Providing Patient Satisfaction

Interestingly, there has been little in the way of investigation comparing patient satisfaction with one anesthetic technique versus another. In White’s 1983 study, an intravenous bolus technique was compared to an infusion technique for both a fentanyl-based and a ketamine-based anesthetic, and satisfaction among the various groups was virtually indistinguishable. The largest study comparing patient satisfaction with anesthesia was published by Perrott, et al. in 2003. In a sample of over 34,000 patients, patient satisfaction approached 95% overall with no
significant difference in satisfaction between the conscious sedation group (94.4%) and the general anesthesia/deep sedation group (94.9%). Interestingly, virtually all of patients who received general anesthesia or deep sedation first received a pre-induction dose of midazolam, the same primary sedating agent used in the conscious sedation category. Consequently, when a patient receives a few milligrams of midazolam as a pre-induction agent, it appears to make little difference in his or her satisfaction with the anesthetic, regardless of the subsequent anesthetic technique.

In another article from the same large study a table was compiled comparing all of the various combinations of the intravenous agents utilized in a wide range of anesthetic techniques. It was found that all techniques relied upon a pre-induction dose of benzodiazepine (usually midazolam). The satisfaction rate for all of the combination categories was 95% to 96%. Respondents in the study were not asked to indicate whether their anesthetics were delivered by an intermittent bolus or by an infusion pump. However, because no difference in satisfaction was noted among the various combinations of agents, it is exceedingly unlikely that attempting to distinguish between those anesthetics delivered with the bolus technique or by an infusion-pump technique would have made any difference.

MAINTAINING HEMODYNAMIC STABILITY

By the closing decade of the 20th century most investigators in medical anesthesia and anesthesia for oral and maxillofacial surgery, had concluded that the newer agents such as propofol and remifentanil are best delivered via continuous infusion. In a multicenter evaluation with a cohort of 161 patients who received total intravenous anesthesia with remifentanil and propofol via continuous infusion Hogue, et al. concluded that “remifentanil 0.25-4.0 µg/kg/min. effectively controlled intraoperative responses while allowing for rapid emergence from anesthesia.”

Further studies have tended to be conducted with this administration modality. In 2002, Gansberg, et al. reported that remifentanil used for conscious sedation administered by constant infusion allowed less fluctuation in cardiovascular parameters. Although these studies pointed to the distinct advantages of adding remifentanil to the mix with a continuous infusion, doing so with an intermittent bolus technique was found to be fraught with difficulties. In 2003, a study of 64 subjects who received remifentanil with an intermittent-bolus approach found that “the older cohort (and some younger subjects) experienced…substantial respiratory depression at lower doses.”

In 2012, Kramer, et al. compared a combination of propofol with fentanyl to a combination of propofol and ketamine for deep sedation for third molar surgery. Each of the combinations was delivered with an infusion pump, and both groups demonstrated excellent hemodynamic and respiratory stability. In the propofol-ketamine group there was an overall slight increase in heart rate, but this was not clinically significant.

Also in 2012, Cillo reported on propofol
with low dose ketamine admixtures for dentoalveolar surgery.\textsuperscript{44} The admixtures ranged from a ratio of 10:1 propofol to ketamine to 3.3:1, and all were delivered with an infusion pump. There was excellent hemodynamic stability in the 10:1 and 5:1 ratio groups, which had been previously studied. Only in the higher ketamine concentration group, with a ratio of 3.3:1, was there a significant increase in cardiovascular parameters.

**ASSURING PATIENT SAFETY**

**Infusion Pump Safety**

The safety of any method of drug delivery is obviously essential. Today there is a wide range of infusion devices used in medicine. They are used in intensive care, for patient controlled analgesia, for administration of nutrients, hormones, antibiotics, chemotherapy drugs and insulin, among others. Thus, when one looks at the incidence of adverse events associated with infusion pumps, all these other applications must be taken into account, as well as those that are associated with anesthesia.

Overall, the number of adverse events is quite large. In 2010, the Center for Devices and Radiologic Health of the US Food and Drug Administration mounted an Infusion Pump Improvement Initiative to address reducing the incidence of adverse events.\textsuperscript{10} In it they reported that the FDA had received approximately 56,000 reports of adverse events between 2005 and 2009. The question obviously arises to how many of these events occurred during anesthesia, and what was their impact.

If one wishes to take a detailed look at the setting for adverse events associated with infusion pump reviews, it is difficult to find studies from the United States. Because the United States does not have a national health care system, data has usually been generated from small groups of hospitals as opposed to the nation as a whole. One such study, involving three U.S. hospitals, disclosed that approximately 92% of infusion pump-related errors occurred in the intensive care unit.\textsuperscript{64}

Because data collection from a large U.S. patient population is not possible, one must turn to countries that have national healthcare systems to obtain data generated from relatively large patient samples. Much of the data has been generated in the United Kingdom, Australia and New Zealand.

Obviously, pump-related medication errors are a part of an overall problem of medication errors throughout medicine in general. Intuitively one might expect that having to deal with a piece of medical equipment such as an infusion pump would tend to increase the likelihood of a medication error. In actuality, it appears that exactly the opposite is the case.

In a New Zealand study involving 8,000 anesthetics, 63% of errors involved intravenous boluses while only 20% involved infusions.\textsuperscript{65} Another study in Australia disclosed a 2.5 times greater incidence of drug administration errors via bolus versus infusion.\textsuperscript{66}

An interesting aspect of the introduction
of errors into medication delivery is the underlying cause. In a hospital setting 80% of medication errors are caused by human error as opposed to equipment error. In a United Kingdom study of approximately 1,000 incidents in anesthesia, only 5 involved infusion pumps and most of these were user-related.

In a 2013 review, Cooper and Nossaman examined a number of studies from the world’s literature to better assess the nature of drug errors in anesthesia. The factors identified as being most frequently responsible included failure to read drug vial labels carefully, distraction and inattention. The incidence of pump failure was so low that it did not even appear on the list of causative factors.

The greater incidence of drug errors in bolus administration, as opposed to pump administration, is due to the lack of a double-check and closed loop communication. For example, one can pick up a vial for

Figure 9: Operation of the Aitecs Pro 12S infusion pump: (A) The pump senses the type of syringe and displays the information on the LED screen. (B) Verification that propofol will be the drug delivered. (C) Entering the patient’s weight in kg. (D) Confirming the bolus dose which is one-third of the total induction bolus.
Source: Courtesy of Richard C. Robert, DDS, MS, South San Francisco, CA.
bolus administration without carefully reading the label, draw up the medication and administer it without any double-check whatsoever. Multiple studies point to the importance of a double-check and closed-loop communication.70,71

In keeping with these principles, modern digital infusion pumps have incorporated the confirmation mode discussed in the technology section above (on P. 19). Once a drug administration parameter has been entered into the pump, the entry must be confirmed before the pump will administer the drug. (Fig. 9, p. 24) Thus, there is essentially closed-loop communication between the pump and anesthesia provider. This layer of safe practice can be doubled by have two well-trained personnel review the pump settings before the infusion is delivered. The assistant can do the initial settings and the operator can go back through the settings to assure that they are correct and finally activate the confirmation mode to assure yet a third check.

When pump-related drug errors do occur, two factors are frequently implicated. The first of these is associated with occlusion of the infusion line. If the line becomes occluded and then the occlusion rapidly released, an inadvertent bolus of medication can be administered. This is most frequently encountered when long, small-caliber lines from the pump are at some distance from the patient.8,72 There are multiple sources of pressure that can occlude the line. However, in oral and maxillofacial surgery this problem can easily be circumvented by using a short, larger caliber line kept in plain view. (Fig.10)

A second source of pump-induced medication error is related to changing the vertical height of the pump relative to the patient. This can alter the rate of drug delivery, leading to significant complications for certain drugs such as vasoactive agents.73 The problem is most often encountered in intensive care and hospital-based anesthesia when the patient is being moved from one location to another while the infusion is in progress. In the oral an maxillofacial surgery office, the patient and pump are in static locations, making it exceedingly unlikely that this source of error would be encountered.
Overall, it has been demonstrated that most medication errors can be prevented by systems that incorporate tiers of protection. These include, double-checks, closed-loop communication and checklists for personnel involved in the administration of drugs. The incorporation of an infusion pump into drug delivery is in keeping with these system modifications to assure prevention rather than causation of drug administration errors.

CONVENIENCE AND COST

The evidence base discussed in the sections above suggests that delivery of an intravenous anesthetic via an infusion pump provides better surgical conditions, maximal hemodynamic stability, a higher level of safety along with patient acceptance comparable to the traditional intermittent bolus technique. The two remaining issues in comparing the two approaches are not scientific but practical ones—the ease and cost of administration.

Both ease of administration and cost of infusion pumps have been topics of concern for several decades. In the early 1980s a survey of 2,000 anesthesiologists was conducted in Great Britain and Ireland to determine why so many anesthesia providers had failed to adopt infusion pumps, even though technologic advancements had made them much more practical alternatives than the previously available bulky, expensive pumps. The two primary reasons cited were the time to set up the infusion and the cost of the equipment.

As the decade progressed, newer, simpler, easy-to-program pumps became available, propofol entered the market and innumerable scientific studies enforced the concept of the maintenance of the constant serum level for optimal expression of drug attributes. By the end of the 1980s, Paul White, then with the department of anesthesiology at the Washington University School of Medicine and a major contributor to the literature for ambulatory anesthesia, opined “in the near future infusion will likely become standard equipment on all anesthesia machines and anesthesiologists should find these techniques easier to use in their clinical practice.” A review of the literature suggests that many share Dr. White’s opinion. During the 1990s and thereafter fewer and fewer reports of studies conducted with the intermittent-bolus technique were published.

As the new millennium arrived, the evidence base discussed above convinced the majority of anesthesiologists worldwide that providing intravenous anesthesia with a constant infusion provided by an infusion pump was the only prudent course for them to follow. Investigators in the field of dental and oral and maxillofacial surgery anesthesia have unquestionably followed the lead of their medical anesthesia colleagues.

However, it is apparent that oral and maxillofacial surgeons in a private practice setting have remained unconvinced. Although infusion pumps have become relatively standard components of anesthetic studies and university-based oral and maxillofacial surgery anesthesia training, private practice surgeons have been slow to come to the realization that most of the previous problems with pump usage have been largely overcome.
Earlier we described the two primary arguments against pump usage: ease of administration and pump cost. The ease of administration issue has very simple solutions for the office-based surgeon. State-of-the-art infusion pumps are compact and exceedingly easy to program. They can be easily attached to the operating chair and no longer require any special lines or attachment devices. (Fig. 10, P. 25) They take standard syringes of various sizes from 10 mL to 60 mL. In addition, these new smart pumps actually flawlessly detect both the brand and volume of the syringe when it is attached to the pump. This information is then displayed on a LED screen for the operator to confirm (Fig. 9A, P. 24). Because the syringes and connectors are the same ones used for the average intermittent bolus technique, there is no longer any appreciable difference in the convenience and expense of the “plumbing.” For the same cost and investment of time, the anesthesia provider also gets the added safety feature of confirmation mode to assure that the appropriate dosage of drug will be delivered and at the appropriate rate.

Another “plumbing” issue is the small volume of anesthetic agent with which the pump is primed. The connecting tubing usually holds a few mL’s of anesthetic that would potentially go unused when the plunger of the syringe reaches zero. However, if just another 20-30 mg (2-3 mL) of agent is needed at the end of the case, there is no need to open a new vial. One merely places a 10 cc syringe filled with IV fluid obtained from the patient’s IV bag to replace the syringe used for the agent. The IV fluid propels the remaining several cc’s of anesthetic solution into the IV line and the procedure can be completed without the expense of opening up a new vial of anesthetic.38

The final cost impediment is obviously the cost of the pump itself. Several decades ago medical anesthesiologists were also reluctant to adopt infusion pumps because of their expense. They obviously found that the enumerable advantages of using an infusion pump (discussed earlier in this section) outweighed the cost saving issue. In addition, in most settings the infusion pump actually pays for itself.

In a recent study, Kramer, et al. alluded to an important cost saving that can accompany pump utilization.63 With the newer short duration-of-action anesthetic agents such as propofol and remifentanil, a combination approach can be quite efficacious. They found that the propofol-remifentanil combination provided more rapid recovery and earlier return to “street readiness” than a propofol-ketamine approach. The shorter recovery time could reduce the cost of office personnel required for recovering patients. Trying to maintain a relatively constant serum level of anesthetic consisting of both propofol and remifentanil is difficult using an intermittent bolus technique. However, with an infusion pump the two drugs can be delivered concomitantly at a constant rate.

Although oral and maxillofacial surgeons seem to balk at the $2,000-$3,000 expense of the infusion pump, they appear to be quite willing to spend $50,000 on a new digital panograph or well over a $100,000 for a cone-beam CT machine. They do so because
there is a perceived benefit in improved visualization that leads to better surgery. Should not the same rationale apply to a comparatively minor expense of an infusion pump? There is a huge mass of literature which substantiates the better working conditions, hemodynamic stability and safety that accompanies use of an infusion pump for intravenous anesthesia.

Just as in the case of the radiographic equipment discussed above, the cost are rapidly recouped. In most states the fee for intravenous anesthesia is several hundred dollars per case. If the surgeon were to make a small increase in anesthesia fee of approximately $3.00 per case (approximately 1%), the average surgeon would recoup the expense of the pump within a single year. Thus, it would appear that oral and maxillofacial surgeons’ failure to adopt the standard practice of our medical anesthesia colleagues is indeed “penny-wise, but pound foolish.”

CONCLUSION

In this section I have conducted a comprehensive review of the rationale that has prompted medical anesthesia providers to adopt infusion pumps for delivery of total intravenous anesthesia. I have also described the time lag between the acceptance of new agents and techniques by anesthesiologists before oral and maxillofacial surgeons follow suit. Early on, anesthesiologists saw the logic of replacing diazepam with midazolam, meperidine with fentanyl and the barbiturate anesthetic agents thiopental and methohexital with propofol, several years before their oral and maxillofacial surgery colleagues. It was not until the so-called “Brevital Crisis” in the early years of the first decade of the new century that oral and maxillofacial surgeons were finally forced to adopt propofol as their primary intravenous anesthetic.

Are we not now at another turning point in office-based anesthesia in oral and maxillofacial surgery? We are besieged by pressures from the outside regarding the safety and appropriateness of our anesthetic approach. Many of those leveling criticism come from an anesthesia background that long ago adopted infusion pumps as their standard form of anesthetic delivery for TIVA. If we fail to adopt what is considered to be a standard part of ambulatory anesthesia practice, we leave ourselves far more open to the criticism that we are utilizing an antiquated approach.

Without question the intermittent-bolus technique revolutionized office-based anesthesia in oral and maxillofacial surgery during the middle of the last century. It has been utilized safely and efficiently for the anesthesia of millions of patients for over half a century. However, during that half-century, significant advancements in pharmacology and technology have provided an avenue for an even better anesthetic with a solid evidence base behind it.

It is my opinion that if Adrian Hubbell were alive today, he would embrace this new technology without question. When methohexital became available with a shorter duration of action, he readily made the change from sodium pentothal to the new agent to capitalize on its advantages. When it became obvious that delivering frequent boluses
of anesthetics with syringes and needles was time-consuming and cumbersome, he developed his human-powered pump, the “Hubbell Bubble.” If he could see that an even

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